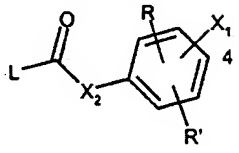
Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application.

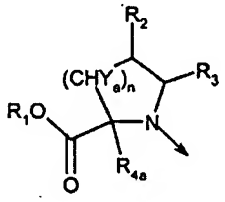
Listing of Claims

1. (Currently Amended) A compound of the formula



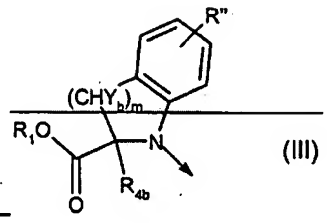
(I)

wherein L is a radical selected from



(II)

-or-



(III)

in which

R_1 is hydrogen, optionally substituted alkyl, aryl, heteroaryl, aralkyl or cycloalkyl;

R_2 is hydrogen, hydroxy, oxo, optionally substituted alkyl, aryl, aralkyl, alkoxy, aryloxy, aralkoxy, alkylthio, arylthio or aralkylthio;

R_3 is hydrogen; or

R_2 and R_3 combined are alkylene which together with the carbon atoms to which they are attached form a fused 5- to 7-membered ring; or

R_2 and R_3 combined are a bond between the carbon atoms to which they are attached;

n is zero or an integer of 1 or 2;

Y_a is hydrogen; or

Y_a and R_2 combined are a bond between the carbon atoms to which they are attached;

R_{4a} is hydrogen; or

R_{4a} and Y_a combined are a bond between the carbon atoms to which they are attached;

~~R" is hydrogen, optionally substituted alkyl, alkoxy or halogen;~~

~~m is an integer of 1 or 2;~~

~~Y_b is hydrogen;~~

~~R_{4b} is hydrogen; or~~

~~R_{4b} and Y_b combined are a bond between the carbon atoms to which they are attached;~~

R and R' are independently hydrogen, halogen, optionally substituted alkyl, alkoxy, aralkyl or heteroaralkyl; or

R and R' combined together with the carbon atoms to which they are attached form an optionally substituted fused 5- to 6-membered aromatic or heteroaromatic ring provided that R and R' are attached to carbon atoms adjacent to each other; or

R-C and R'-C may independently be replaced by nitrogen;

X_1 is $-Z-(CH_2)_p-Q-W$ wherein

Z is a bond, O, S, S(O) or $S(O)_2$; or

Z is $-C(O)NR_5-$ in which

R_5 is hydrogen, alkyl or aralkyl;

p is an integer from 1 to 8;

Q is a bond; or

Q is $-O(CH_2)_r-$ or $-S(CH_2)_r-$ in which

r is zero or an integer from 1 to 8; or

Q is $-O(CH_2)_{1-8}O-$, $-S(CH_2)_{1-8}O-$, $-S(CH_2)_{1-8}S-$ or -C(O)-; or

Q is $-C(O)NR_6-$ in which

R_6 is hydrogen, optionally substituted alkyl, cycloalkyl, aryl, heteroaryl, aralkyl or heteroaralkyl; or

Q is $-NR_7-$, $-NR_7C(O)-$, $-NR_7C(O)NR_8-$ or $-NR_7C(O)O-$ in which

R_7 is hydrogen, optionally substituted alkyl, cycloalkyl, aryl, heteroaryl, aralkyl or heteroaralkyl;

R_8 is hydrogen, alkyl or aralkyl;

W is <u>oxazole</u> ~~cycloalkyl, aryl, heterocyclyl, aralkyl or heteroaralkyl; or~~

~~W and R_6 taken together with the nitrogen atom to which they are attached form a 8- to 12-membered bicyclic ring, which may be optionally substituted or may contain another heteroatom selected from oxygen, nitrogen and sulfur;~~

X_2 is $-C(R_9)_2-$, O , S or $-NR_{10}-$ in which

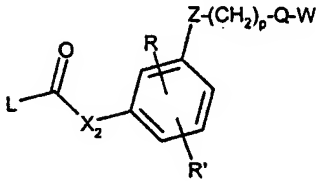
R_9 is hydrogen or lower alkyl;

R_{10} is hydrogen, alkyl or aralkyl;

~~provided that W is not 2-methylquinolin-4-yl when Z is O, p is 1, Q is a bond, X_2 is $-C(R_9)_2-$ in which R_9 is hydrogen, and X_4 is located at the 4-position; or W is not 2-butyl-4-chloro-5-hydroxymethylimidazol-1-yl when Z is a bond, p is 1, Q is a bond, X_2 is $-NR_{10}-$ in which R_{10} is hydrogen, and X_4 is located at the 4-position;~~

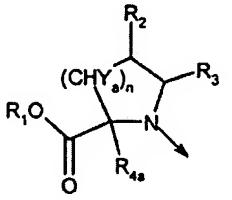
or an optical isomer thereof; or a mixture of optical isomers thereof; or a pharmaceutically acceptable salt thereof.

2. (Currently Amended) The compound according to claim 1 of the formula

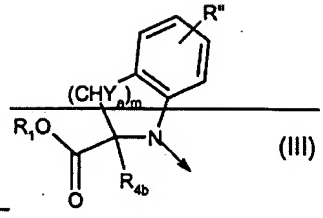


(IA)

wherein L is a radical selected from:



(II)



(III)

~~or~~

in which

R_1 is hydrogen, optionally substituted alkyl, aryl, heteroaryl, aralkyl or cycloalkyl;

R_2 is hydrogen, hydroxy, oxo, optionally substituted alkyl, aryl, aralkyl, alkoxy, aryloxy, aralkoxy, alkylthio, arylthio or aralkylthio;

R_3 is hydrogen; or

R_2 and R_3 combined are alkylene which together with the carbon atoms to which they are attached form a fused 5- to 7-membered ring; or

R_2 and R_3 combined are a bond between the carbon atoms to which they are attached;

n is 1;

Y_a is hydrogen; or

Y_a and R_2 combined are a bond between the carbon atoms to which they are attached;

R_{4a} is hydrogen; or

R_{4a} and Y_a combined are a bond between the carbon atoms to which they are attached;

~~R'' is hydrogen, optionally substituted alkyl, alkoxy or halogen;~~

~~m is 1;~~

~~Y_b is hydrogen;~~

~~R_{4b} is hydrogen; or~~

~~R_{4b} and Y_b combined are a bond between the carbon atoms to which they are attached;~~

R and R' are independently hydrogen, halogen, optionally substituted alkyl, alkoxy, aralkyl or heteroaralkyl; or

R and R' combined together with the carbon atoms to which they are attached form an optionally substituted fused 5- to 6-membered aromatic or heteroaromatic ring provided that R and R' are attached to carbon atoms adjacent to each other; or

Z is a bond, O or S;

p is an integer from 1 to 8;

Q is a bond; or

Q is $-O(CH_2)_r-$ or $-S(CH_2)_r-$ in which

r is zero or an integer from 1 to 8; or

Q is $-C(O)NR_6-$ in which

R_6 is hydrogen, optionally substituted alkyl, cycloalkyl, aryl, heteroaryl, aralkyl or heteroaralkyl; or

Q is $-NR_7-$, $-NR_7C(O)-$, $-NR_7C(O)NR_8-$ or $-NR_7C(O)O-$ in which

R_7 is hydrogen, optionally substituted alkyl, cycloalkyl, aryl, heteroaryl, aralkyl or heteroaralkyl;

R_8 is hydrogen, alkyl or aralkyl;

W is oxazole ~~cycloalkyl, aryl, heterocyclyl, aralkyl or heteroaralkyl; or~~

~~W and R_6 taken together with the nitrogen atom to which they are attached form a 8- to 12-membered bicyclic ring, which may be optionally substituted or may contain another heteroatom selected from oxygen, nitrogen and sulfur~~;

X_2 is $-C(R_9)_2-$, O , S or $-NR_{10}-$ in which

R_9 is hydrogen or lower alkyl;

R_{10} is hydrogen or lower alkyl;

or an optical isomer thereof; or a mixture of optical isomers thereof; or a pharmaceutically acceptable salt thereof.

3. (Currently Amended) The compound according to claim 2, wherein

R_1 is hydrogen or optionally substituted alkyl;

R_2 and R_3 are hydrogen;

Y_a is ~~and Y_b are~~ hydrogen;

R_{4a} is ~~and R_{4b} are~~ hydrogen;

R and R' are independently hydrogen, halogen, optionally substituted C_{1-6} alkyl or C_{1-6} alkoxy;

p is an integer from 1 to 5;

Q is a bond; or

Q is $-O(CH_2)_r-$ or $-S(CH_2)_r-$ in which

r is zero or 1; or

Q is $-C(O)NR_6-$ in which

R_6 is hydrogen or lower alkyl; or

Q is $-NR_7-$, $-NR_7C(O)-$, $-NR_7C(O)NR_8-$ or $-NR_7C(O)O-$ in which

R_7 is hydrogen or optionally substituted alkyl;

R_8 is hydrogen or alkyl;

X_2 is $-C(R_9)_2-$, O , S or $-NR_{10}-$ in which

R_9 is hydrogen or methyl;

R_{10} is hydrogen;

or an optical isomer thereof; or a mixture of optical isomers thereof; or a pharmaceutically acceptable salt thereof.

4. (Currently Amended) The compound according to claim 3, wherein

R_7 and R' ~~and R"~~ are hydrogen;

Q is a bond; or

Q is $-O(CH_2)_r-$ or $-S(CH_2)_r-$ in which

r is zero; or

Q is $-NR_7-$, $-NR_7C(O)-$, $-NR_7C(O)NR_8-$ or $-NR_7C(O)O-$ in which

R_7 is hydrogen or optionally substituted lower alkyl;

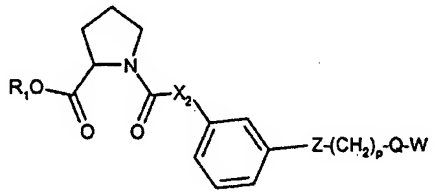
~~W is cycloalkyl, aryl or heterocyclyl;~~

or an optical isomer thereof; or a mixture of optical isomers thereof; or a pharmaceutically acceptable salt thereof.

5. (Previously Presented) The compound according to claim 4, wherein the asymmetric center in radical L is in the (R) configuration; or a pharmaceutically acceptable salt thereof.

6. (Previously Presented) The compound according to claim 4, wherein X_2 is $-C(R_9)_2-$ in which R_9 is methyl; or a pharmaceutically acceptable salt thereof; or an optical isomer thereof; or a mixture of optical isomers thereof.

7. (Currently Amended) The compound according to claim 4 of the formula



(IB)

wherein

R_1 is hydrogen or optionally substituted alkyl;

Z is a bond, O or S;

p is an integer from 1 to 3;

Q is a bond, O or S; or

Q is $-NR_7C(O)-$ in which

R_7 is hydrogen or optionally substituted lower alkyl;

W is oxazole ~~aryl or heterocyclyl~~;

X_2 is $-C(R_9)_2-$, O , S or -NH- in which

R_9 is hydrogen or methyl;

or an optical isomer thereof; or a mixture of optical isomers thereof; or a pharmaceutically acceptable salt thereof.

8. (Cancelled)

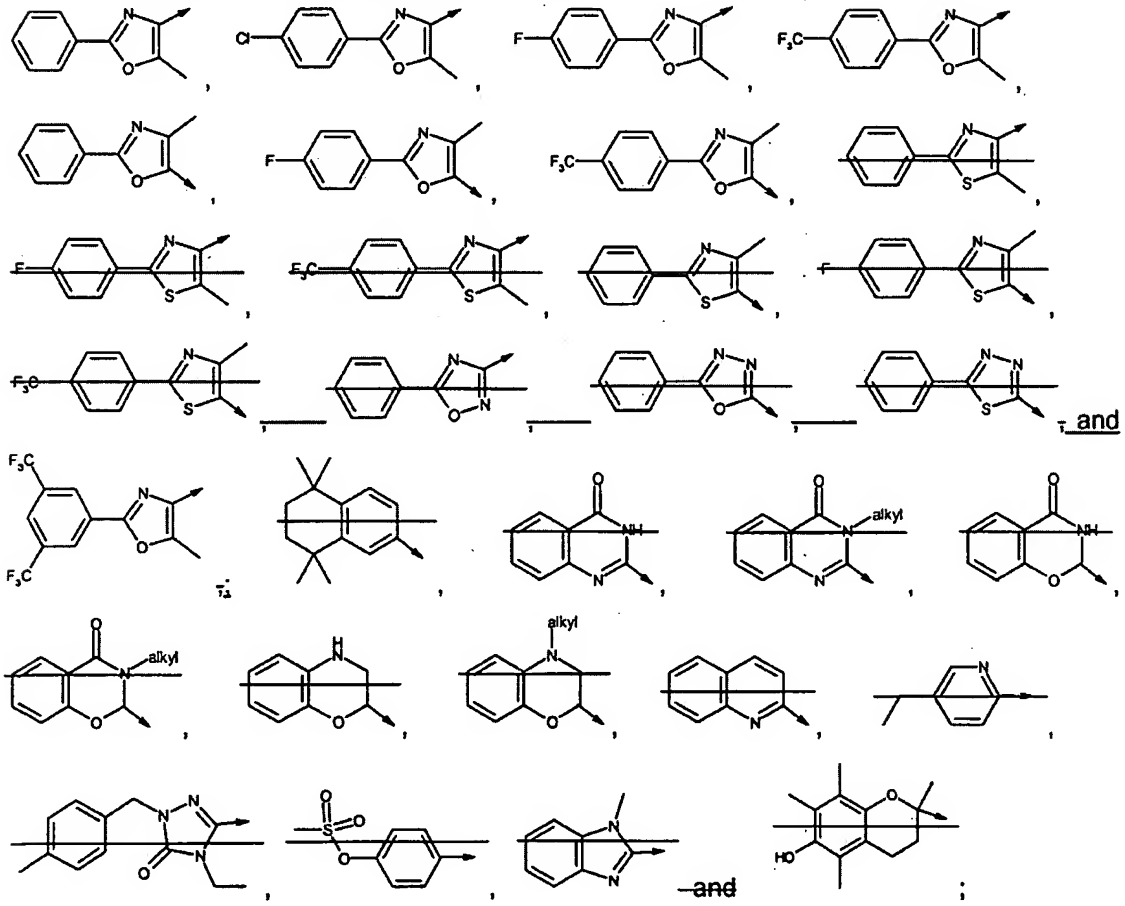
9. (Currently Amended) The compound according to claim 7, wherein

Z is bond, O or S;

p is an integer of 1 or 2;

Q is a bond;

W is selected from the group consisting of:



or an optical isomer thereof; or a mixture of optical isomers thereof; or a pharmaceutically acceptable salt thereof.

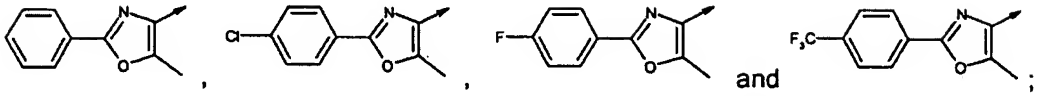
10 (Previously Presented) The compound according to claim 9, wherein

Z is O;

p is 1;

X_2 is $-C(R_9)_2-$ in which R_9 is methyl;

W is selected from the group consisting of:



and ;

or an optical isomer thereof; or a mixture of optical isomers thereof; or a pharmaceutically acceptable salt thereof.

11. (Previously Presented) The compound according to claim 10, wherein the asymmetric center in radical L is in the (R) configuration; or a pharmaceutically acceptable salt thereof.

12. (Cancelled)

13. (Currently Amended) The compound according to claim 7, wherein

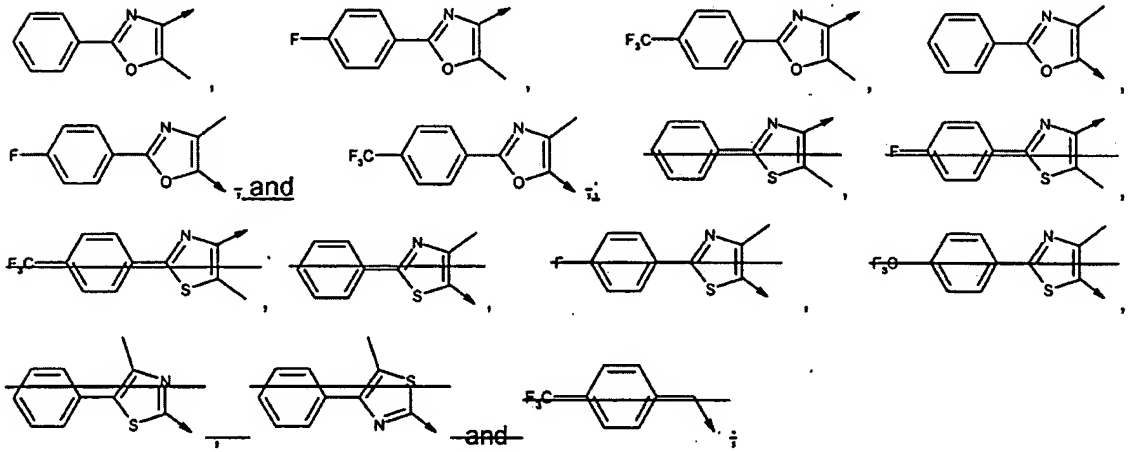
Z is a bond;

p is 1;

Q is $-NR_7C(O)-$ in which

R_7 is hydrogen or methyl;

W is selected from the group consisting of:



and

or an optical isomer thereof; or a mixture of optical isomers thereof; or a pharmaceutically acceptable salt thereof.

14 – 20. (Cancelled)

21. (Currently Amended) The compound according to claim 1 which is selected from:

(R)-1-{2-[3-(5-Methyl-2-phenyl-oxazol-4-ylmethoxy)-phenyl]-acetyl}-pyrrolidine-2-carboxylic acid;

(R)-1-[3-(5-Methyl-2-phenyl-oxazol-4-ylmethoxy)-phenylsulfanylcarbonyl]-pyrrolidine-2-carboxylic acid;

(R)-Pyrrolidine-1,2-dicarboxylic acid-1-[3-(5-methyl-2-phenyl-oxazol-4-ylmethoxy)-phenyl] ester;

(R)-1-{2-Methyl-2-[3-(5-methyl-2-phenyl-oxazol-4-ylmethoxy)-phenyl]-propionyl}-pyrrolidine-2-carboxylic acid;

(R)-1-{2-[4-(5-Methyl-2-phenyl-oxazol-4-ylmethoxy)-phenyl]-acetyl}-pyrrolidine-2-carboxylic acid;

(R)-1-{2-[4-(5-Methyl-2-phenyl-oxazol-4-ylmethoxy)-phenyl]-acetyl}-pyrrolidine-2-carboxylic acid;

(R)-1-(2-{3-[2-(4-Carbamoylphenyl)-5-methyl-oxazol-4-ylmethoxy]-phenyl}-2-methyl-propionyl)-pyrrolidine-2-carboxylic acid;

(R)-1-(2-{3-[2-(4-Cyano-phenyl)-5-methyl-oxazol-4-ylmethoxy] phenyl}-2-methyl-propionyl)-pyrrolidine-2-carboxylic acid;

(R)-1-(2-{3-[2-(4-Chloro-3-fluoro-phenyl)-5-methyl-oxazol-4-yl-methoxy]-phenyl}-2-methyl-propionyl)-pyrrolidine-2-carboxylic acid;

~~(R)-1-{2-Methyl-2-[4-({methyl-[2-(4-trifluoromethyl-phenyl)-acetyl]-amino}-methyl)-phenyl]-propionyl}-pyrrolidine-2-carboxylic acid;~~

(R)-1-(2-{3-[2-(4-Fluoro-phenyl)-5-methyl-oxazol-4-ylmethoxy]-4-methoxy-phenyl}-2-methyl-propionyl)-pyrrolidine-2-carboxylic acid;

(R)-1-(2-{3-[2-(4-Chloro-phenyl)-5-methyl-oxazol-4-ylmethoxy]-phenyl}-2-methyl-propionyl)-pyrrolidine-2-carboxylic acid;

(R)-1-{2-Methyl-2-[3-(5-methyl-2-p-tolyl-oxazol-4-ylmethoxy)-phenyl]-propionyl}-pyrrolidine-2-carboxylic acid;

~~(R)-1-[2-(4-{2-[2-(4-Trifluoromethyl-phenyl)-acetylamino]-ethyl}-phenyl)-acetyl]-pyrrolidine-2-carboxylic acid;~~

(R)-1-(2-Methyl-2-{3-[5-methyl-2-(4-trifluoromethyl-phenyl)-oxazol-4-ylmethoxy]-phenyl}-propionyl)-pyrrolidine-2-carboxylic acid;

(R)-1-(2-{3-[2-(4-Fluoro-phenyl)-5-methyl-oxazol-4-ylmethoxy]-phenyl}-2-methyl-propionyl)-pyrrolidine-2-carboxylic acid;

(R)-1-(2-{3-[2-(5-Methyl-2-phenyl-oxazol-4-yl)-ethyl]-phenyl}-acetyl)-pyrrolidine-2-carboxylic acid;

~~(R)-1-[2-(3-{[(4-Methyl-5-phenyl-thiazole-2-carbonyl)-amino]-methyl}-phenyl)-acetyl]-pyrrolidine-2-carboxylic acid;~~

~~(R)-1-[2-Methyl-2-(3-{[(4-methyl-2-phenyl-thiazole-5-carbonyl)-amino]-methyl}-phenyl)-propionyl]-pyrrolidine-2-carboxylic acid;~~

~~(R)-1-[2-(3-{[(4-Methyl-2-phenyl-thiazole-5-carbonyl)-amino]-methyl}-phenyl)-acetyl]-pyrrolidine-2-carboxylic acid;~~

~~(R)-1-{2-[3-(1-Benzyl-4-ethyl-5-oxo-4,5-dihydro-1H-[1,2,4]triazol-3-ylmethoxy)-phenyl]-acetyl}-pyrrolidine-2-carboxylic acid;~~

(R)-1-(2-{3-[2-(5-Methyl-2-phenyl-oxazol-4-yl)-ethoxy]-phenyl}-acetyl)-pyrrolidine-2-carboxylic acid;

(R)-1-(2-{3-[5-Methyl-2-(4-trifluoromethyl-phenyl)-oxazol-4-ylmethoxy]-phenyl}-acetyl)-pyrrolidine-2-carboxylic acid;

(S)-1-{2-[3-(5-Methyl-2-phenyl-oxazol-4-ylmethoxy)-phenyl]-acetyl}-pyrrolidine-2-carboxylic acid;

~~(R)-1-{2-[3-(4-Methyl-benzyloxy)-phenyl]-acetyl}-pyrrolidine-2-carboxylic acid;~~

~~(R)-1-{2-Methyl-2-[3-(5-methyl-2-phenyl-oxazol-4-ylmethoxy)-phenyl]-propionyl}-2,3-dihydro-1H-indole-2-carboxylic acid;~~

~~(R)-1-(2-{3-[2-(4-Carbamoyl-phenyl)-5-methyl-oxazol-4-ylmethoxy]-phenyl}-2-methyl-propionyl)-2,3-dihydro-1H-indole-2-carboxylic acid;~~

~~(R)-1-(2-{3-[2-(4-Chloro-3-fluoro-phenyl)-5-methyl-oxazol-4-ylmethoxy]-phenyl}-2-methyl-propionyl)-2,3-dihydro-1H-indole-2-carboxylic acid;~~

~~(R)-1-(2-{3-[2-(4-Cyano-phenyl)-5-methyl-oxazol-4-ylmethoxy]-phenyl}-2-methyl-propionyl)-2,3-dihydro-1H-indole-2-carboxylic acid;~~

~~(R)-1-(2-{3-[2-(4-Fluoro-phenyl)-5-methyl-oxazol-4-ylmethoxy]-4-methoxy-phenyl}-2-methyl-propionyl)-2,3-dihydro-1H-indole-2-carboxylic acid;~~

~~(R)-1-{2-Methyl-2-[3-(5-methyl-2-p-tolyl-oxazol-4-ylmethoxy)-phenyl]-propionyl}-2,3-dihydro-1H-indole-2-carboxylic acid;~~

~~(R)-1-(2-Methyl-2-{3-[5-methyl-2-(4-trifluoromethyl-phenyl)-oxazol-4-ylmethoxy]-phenyl}-propionyl)-2,3-dihydro-1H-indole-2-carboxylic acid;~~

~~(R)-1-(2-{3-[2-(4-Chloro-phenyl)-5-methyl-oxazol-4-ylmethoxy]-phenyl}-2-methyl-propionyl)-2,3-dihydro-1H-indole-2-carboxylic acid; and~~

~~(R)-1-(2-{3-[2-(4-Fluoro-phenyl)-5-methyl-oxazol-4-ylmethoxy]-phenyl}-2-methyl-propionyl)-2,3-dihydro-1H-indole-2-carboxylic acid;~~

or an optical isomer thereof; or a mixture of optical isomers thereof; or a pharmaceutically acceptable salt thereof.

22. (Previously Presented) A method for the activation of Peroxisome Proliferator-Activated Receptors (PPARs), comprising:

administering to a mammal in need thereof a therapeutically effective amount of a compound of claim 1.

23. (Previously Presented) A method for the treatment of conditions mediated by PPARs, comprising:

administering to a mammal in need thereof a therapeutically effective amount of a compound of claim 1.

24. (Previously Presented) The method according to claim 23, further comprising:

administering said compound in combination with a therapeutically effective amount of insulin, insulin derivative or mimetic; insulin secretagogue; insulinotropic sulfonylurea receptor ligand; insulin sensitizer; biguanide; alpha-glucosidase inhibitors; GLP-1, GLP-1 analog or mimetic; DPPIV inhibitor; HMG-CoA reductase inhibitor; squalene synthase inhibitor; FXR or LXR ligand; cholestyramine; fibrates; nicotinic acid or aspirin.

25. (Previously Presented) The method of claim 23, wherein the condition mediated by PPARs is dyslipidemia, hyperlipidemia, hypercholesteremia, atherosclerosis, hypertriglyceridemia, heart failure, myocardial infarction, vascular diseases, cardiovascular diseases, hypertension, obesity, inflammation, arthritis, cancer, Alzheimer's disease, skin disorders, respiratory diseases, ophthalmic disorders, inflammatory bowel diseases, ulcerative colitis and Crohn's disease, Syndrome-X, and type-1 or type-2 diabetes.

26. (Previously Presented) A pharmaceutical composition, comprising:

a therapeutically effective amount of a compound of claim 1 in combination with one or more pharmaceutically acceptable carriers.

27. (Currently Amended) The pharmaceutical composition according to claim ~~25~~ 26 further comprising the therapeutically effective amount of a compound in combination with a therapeutically effective amount of insulin, insulin derivative or mimetic; insulin secretagogue; insulinotropic sulfonylurea receptor ligand; insulin sensitizer; biguanide; alpha-glucosidase inhibitors; GLP-1, GLP-1 analog or mimetic; DPPIV inhibitor; HMG-CoA reductase inhibitor; squalene synthase inhibitor; FXR or LXR ligand; cholestyramine; fibrates; nicotinic acid; or aspirin.

28 – 34. (Cancelled)